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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Our Ref: 1038-384 MIS:as

In re patent application

No.	08/286,189
Applicant:	Sonia E. Sanhueza et al
Title:	INACTIVATED RESPIRATORY SYNCYTIAL VIRAL VACCINES
Filed:	August 5, 1994
Group No:	1648
Examiner:	J. Parkin

March 24, 2000

BY COURIER

The Commissioner of Patents
and Trademarks,
Washington, D.C. 20231,
U.S.A.

Dear Sir:

This Communication is in response to the Office Action of September 27, 1999.

Petition is hereby made under the provisions of 37 CFR 1.136(a) for an extension of three months of the period for response to the outstanding Office Action on this case. We enclose our cheque in the amount of the prescribed fees.

The courtesy of the Examiner in granting an Interview on this application to the applicant's representative, Mr. Michael Stewart, and to Mr. Reza Yacoob of the Patents Department of the Assignee, Connaught Laboratories Limited, is much appreciated. It is felt that the Interview was material in advancing the prosecution of this application. The Interview Summary Record fairly sets forth the discussion at the Interview. The comments and submissions herein complement and supplement those made to the Examiner at the Interview.

The Examiner rejected claims 1, 3 to 9 and 11 to 16 under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

As the Examiner correctly points out, the present invention is directed to RSV vaccine compositions that are capable of inducing non-immunopotentiating and protective immune responses in humans, their methods of preparation and immunization methods employing said vaccine compositions.

As the Examiner correctly states, applicants evaluated their RSV preparation in cotton rats and concluded that the inactivated RSV preparation elicited protective immune responses in the cotton rat without causing the exacerbated pulmonary pathology associated with other putative vaccine compositions. The Examiner does not appear to question these conclusions.

The Examiner's rejection appears to be based on the statement contained in the Office Action that:

> "The disclosure fails to provide data from an art-recognized animal model. ... the skilled artisan ... would reasonably conclude that the cotton rat model does not represent a reasonable system for assessing the efficacy of a putative human RSV vaccine."

On the contrary, the cotton rat used in applicants experimentation is the scientifically-accepted animal model of efficacy of a range of respiratory viruses, including RSV. The Examiner has quoted from a number of literature references, including Hall, 1994; Toms, 1995; Murphy et al, 1994; Salkind and Roberts, 1992; and Tristram et al, 1993, in an attempt to cast doubt on the legitimacy of the cotton rat as the appropriate animal model. Each of these references is a review article concerning the development of an RSV vaccine, the hurdles to be faced and the failures of the past, which is all very interesting.

However, we draw attention to the following:

In WO93/21310, of record herein, the same Murphy as the Murphy et al reference cited by the Examiner, states with certainty:

> " ... based on these studies, it would appear that the cotton rat constitutes a relevant model for predicting the success of an RSV vaccine in infants and small children" (page 10, lines 16 to 18).

Groothuis et al, of record herein, describe the results of prophylactic administration of RSV immune globulin to high-risk infants and young children. It is stated (page 1524, left-hand column):

> "... studies in animals [referencing various Prince et al references, many of which are of record herein] and epidemiologic observations in

> full-term infants indicate that the maintenance of serum titers of respiratory syncytial virus-neutralizing antibody between 1:200 and 1:400 prevents respiratory syncytial virus infection in the lower respiratory tract."

The animal studies, including cotton rat studies, correlate to the epidemiological observations in infants concerning the titer levels necessary to prevent infection.

The reference then goes on to study the use of an intravenous immune globulin containing high titers of RSV-neutralizing antibody in an attempt to attenuate or prevent infection in high-risk children by monthly infusions of this immune globulin during the season of RSV infection. The study concludes (col. 2, Abstract):

> "Administration of high doses of respiratory syncytial virus immune globulin is a safe and effective means of preventing lower respiratory tract infection in infants and young children at high risk for this disease."

This study, therefore, shows the results obtained in cotton rats were supported by data in human trials.

Coe and Prince (Immunology 1996, 88, 323 to 330) is cited for the first time herein. A copy of this reference is attached to the enclosed PTO-1449 listing this article. Our enclosed Deposit Account form is enclosed in respect of the prescribed fee for the submission of a PTO-1449. This reference discusses the cotton rats, noting:

> "Pulmonary pathology produced in cotton rats by these pathogens [including RSV] is similar to that seen in humans. Recent clinical studies with RSV ... have shown a high level of correlation between experimental results in cotton rats and outcomes in clinical trials [referencing Groothuis et al reference referred to above]" (emphasis added).

Having regard thereto, it is submitted that there is an art-accepted correlation of results in cotton rats to results in humans with respect to RSV infection and protection.

Accordingly, it is submitted that claims 1, 3 to 9 and 11 to 16 are fully enabled by the specification and hence the rejection thereof under 35 USC 112, first paragraph, in this regard, should be withdrawn.

It is believed that this application is now in condition for allowance and early and favourable consideration and allowance are respectfully solicited.

Respectfully submitted,

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